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516704

PCT/FR2003/001685

PATENT COOPERATION TREATY



Translation

PCT

Rec'd PCT/PTO 02 DEC 2004

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

10/5167U4

Applicant's or agent's file reference SSL0093-1/DM	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR2003/001685	International filing date (day/month/year) 05 juin 2003 (05.06.2003)	Priority date (day/month/year) 07 juin 2002 (07.06.2002)
International Patent Classification (IPC) or national classification and IPC C07D 417/14, 401/14, A61K 31/497, A61P 25/28		
Applicant SANOFI-AVENTIS		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 19 décembre 2003 (19.12.2003)	Date of completion of this report 19 February 2004 (19.02.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR2003/001685

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

☒ the international application as originally filed

☒ the description:

pages \_\_\_\_\_ 1-68 \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

☒ the claims:

pages \_\_\_\_\_ 1-13 \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, as amended (together with any statement under Article 19  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

☐ the drawings:

pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

☐ the sequence listing part of the description:

pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_  
☐ the claims, Nos. \_\_\_\_\_  
☐ the drawings, sheets/fig \_\_\_\_\_

### 5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR 03/01685

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims	1-13	YES
	Claims		NO
Inventive step (IS)	Claims	1-13	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-13	YES
	Claims		NO

**2. Citations and explanations**

The following documents will be used throughout the procedure:

D1: FR-A-2 803 593;

D2: WO 00/69829 A.

**Novelty:**

Claims 1-13 of the present application fulfil the requirements set forth in PCT Article 33(2) because their subject matter is novel. Documents D1 and D2 disclose only compounds with structures that are not particularly similar. The compounds of D1 and the compounds of the present application differ by virtue of the presence of the double bond in the piperidine ring, the presence of a carbonyl grouping and of piperazine instead of a benzothiophene or benzofuran grouping. D2 discloses compounds that are entirely different because they are all based on a tricyclic skeleton.

**Inventive step:**

D1 describes compounds that have TNF activity and does not

mention any p75 receptors. D2, which is considered to be the closest prior art, describes compounds that have an activity with respect to the p75 receptor. As indicated above, the structures of the compounds of D2 differ from those in the present invention. The technical problem is that of producing compounds that have an activity with respect to the p75 receptor. On the basis of the description and the examples, it can be assumed that all of the compounds as per claim 1 solve the stated technical problem. D2 does not provide any structural indications that would enable a person skilled in the art to produce the same molecules and solve the technical problem. As a result, the invention is not obvious and the requirements set forth in PCT Article 33(3) are met.

# TRAITE DE COOPERATION EN MATIERE DE BREVETS

## PCT

Rec'd PCT/PTO 02 DEC 2004

### RAPPORT D'EXAMEN PRELIMINAIRE INTERNATIONAL



(article 36 et règle 70 du PCT)

10/516704

REC'D 23 FEB 2004

Référence du dossier du déposant ou du mandataire	<b>POUR SUITE A DONNER</b> voir la notification de transmission du rapport d'examen préliminaire international (formulaire PCT/PEA/416)	
Demande internationale No. PCT/FR 03/01685	Date du dépôt international (jour/mois/année) 05.06.2003	Date de priorité (jour/mois/année) 07.06.2002
Classification internationale des brevets (CIB) ou à la fois classification nationale et CIB C07D417/14, C07D417/14		
Déposant SANOFI-SYNTHELABO et al.		

1.	Le présent rapport d'examen préliminaire international, établi par l'administration chargée de l'examen préliminaire international, est transmis au déposant conformément à l'article 36.
2.	Ce RAPPORT comprend 4 feuilles, y compris la présente feuille de couverture.  <input type="checkbox"/> Il est accompagné d'ANNEXES, c'est-à-dire de feuilles de la description, des revendications ou des dessins qui ont été modifiées et qui servent de base au présent rapport ou de feuilles contenant des rectifications faites auprès de l'administration chargée de l'examen préliminaire international (voir la règle 70.16 et l'instruction 607 des Instructions administratives du PCT).  Ces annexes comprennent feuilles.
3.	Le présent rapport contient des indications et les pages correspondantes relatives aux points suivants :  I <input checked="" type="checkbox"/> Base de l'opinion II <input type="checkbox"/> Priorité III <input type="checkbox"/> Absence de formulation d'opinion quant à la nouveauté, l'activité inventive et la possibilité d'application industrielle IV <input type="checkbox"/> Absence d'unité de l'invention V <input checked="" type="checkbox"/> Déclaration motivée selon la règle 66.2(a)(ii) quant à la nouveauté, l'activité inventive et la possibilité d'application industrielle; citations et explications à l'appui de cette déclaration VI <input type="checkbox"/> Certains documents cités VII <input type="checkbox"/> Irrégularités dans la demande internationale VIII <input type="checkbox"/> Observations relatives à la demande internationale

Date de présentation de la demande d'examen préliminaire internationale  19.12.2003	Date d'achèvement du présent rapport  19.02.2004
Nom et adresse postale de l'administration chargée de l'examen préliminaire international   Office européen des brevets D-80298 Munich Tél. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Fonctionnaire autorisé N° de téléphone +49 89 2399-  

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**RAPPORT D'EXAMEN  
PRÉLIMINAIRE INTERNATIONAL**

Demande internationale n°

**PCT/FR 03/01685**

6. Observations complémentaires, le cas échéant :

**V. Déclaration motivée selon l'article 35(2) quant à la nouveauté, l'activité inventive et la possibilité d'application industrielle; citations et explications à l'appui de cette déclaration**

1. Déclaration

Nouveauté

Oui: Revendications 1-13

Non: Revendications

Activité inventive

Oui: Revendications 1-13

Non: Revendications

Possibilité d'application industrielle

Oui: Revendications 1-13

Non: Revendications

2. Citations et explications

**voir feuille séparée**

**RAPPORT D'EXAMEN  
PRELIMINAIRE INTERNATIONAL - FEUILLE SEPARÉE**

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Demande internationale n° PCT/FR 03/01685

**Concernant le point V**

Les documents suivants seront utilisés durant la procédure:

D1: FR-A-2 803 593

D2: WO 00/69829 A

Nouveauté:

Les revendications 1-13 de la présente demande remplissent les conditions énoncées dans l'article 33(2) PCT, leur objet étant nouveau. Les documents D1 et D2 ne divulguent que des composés avec des structures peu similaires. Les composés de D1 et les composés de la présente demande diffèrent de par la présence de la double liaison dans le noyau pipéridinique, la présence d'un groupement carbonyle et de pipérazine au lieu d'un groupement benzothiophène ou benzofurane. D2 divulgue des composés complètement différents, ils sont tous basés sur un squelette tricyclique.

Activité inventive:

D1 décrit des composés avec une activité TNF et ne mentionne pas de récepteur p75. D2, considéré comme état de la technique le plus proche, décrit des composés avec une activité pour récepteur p75. Les structures des composés de D2 diffèrent de la présente invention comme indiqué ci-dessus. Le problème technique est d'obtenir des composés ayant une activité pour récepteur p75. D'après la description et les exemples, on peut supposer que tous les composés selon la revendication 1 résolvent le problème technique posé. D2 ne donne pas d'indications structurales à l'homme du métier pour arriver aux mêmes molécules et résoudre le problème technique. Par conséquent, l'invention n'est pas évidente et les conditions énoncées dans l'article 33(3) PCT sont remplies.